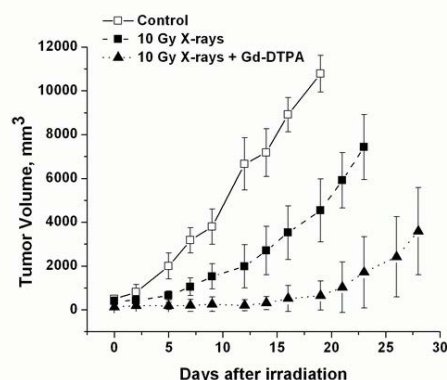


tumor. Attempts of developing tumor targeting drug, which would be capable to deliver necessary amount of high atomic number element into the tumor haven't succeed yet. Another possible way to deliver such elements into the tumor is to utilize some pathological processes caused by tumorigenesis such as blood barrier disruption in case of brain tumors or high vascularization inherent to some tumors. In this work the efficacy of x-rays irradiation with disodium gadopentetate (Gd-DTPA) administration in treating highly vascularized transplanted tumor in mice was studied.

**Material and Methods:** C57BL/6 mice with transplanted adenocarcinoma Ca755 were used in the study. Animals were divided into three groups. 1st group undergo no treatment. 2nd group was irradiated with 10 Gy of x-rays. Animals in 3rd group were administered with 0.3 ml of 0.5M water solution of Gd-DTPA, containing 23 mg of gadolinium and then irradiated as well. Administration of Gd-DTPA was performed with single systemic injection. Irradiation was performed using x-rays generator with anode voltage of 200 kV. Antineoplastic efficacy was estimated by measuring tumor volume and life span of mice.

**Results:** Tumor growth rate plots are presented in Figure.



Tumor growth delay for test group was 13 days whereas in irradiated control group tumor growth delay was just 4 days. Median life span was 22 days, 37 days and 46 days for control group, irradiated control group and test group respectively. In test group 25% of animals have full tumor regression whereas in both control groups no tumor regression was observed. Endpoints of antitumor evaluation, i.e. T/C% ratio and gross log10 tumor cell kill are represented in Table.

Group	T/C, %	Tumor growth delay, days	Gross tumor cell kill log <sub>10</sub>	Antitumor activity (Teicher 2004)
Irradiated control group (irradiation only)	37±6	4	0.5	-
Test group (irradiation + Gd-DTPA injection)	10±3	13	1.6	+++

**Conclusion:** Obtained results show that systemic injection of extracellular drug with gadolinium prior irradiation with x-rays provide enough amount of gadolinium in highly vascularized tumors and lead to significant increase of antineoplastic efficacy of x-rays irradiation.

#### EP-2031

Research on p53 and endostatin gene-radiotherapy induced by EGFR-targeted adenovirus vector in NSCLC  
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**Purpose or Objective:** With the development of molecular biology and gene engineering, more and more attention has been paid to gene-radiotherapy of malignant tumors. The combination of gene therapy and radiotherapy is regarded as

one of the effective methods for the treatment of tumors. This research focused on the Egr-1 promoter with radiation-induced effect, p53 and endostatin genes with function of inducing apoptosis and anti-angiogenesis, and EGFR-targeted adenovirus vector with higher cell infection efficiency. The therapeutic effect of adenovirus vectors Ad.Egr-wtp53-endostatin and Ad.CMV-sCAR-EGF combined with radiotherapy in non-small cell lung cancer is here reported.

**Material and Methods:** The adenovirus vectors Ad.Egr-wtp53-endostatin containing both wild type p53 and antiangiogenic molecule endostatin genes downstream of early growth response-1 (Egr-1) and Ad.CMV-sCAR-EGF containing coxsackie virus receptor extracellular segment (sCAR) and epidermal growth factor (EGF) were constructed using gene recombination technique. The infection efficiency in non-small cell lung cancer cell lines (A549, LK-2 and Lu65) of Ad.Egr-wtp53-endostatin mediated with Ad.CMV-sCAR-EGF expressed fusion protein sCAR-EGF was detected. The expression of wild type p53 and endostatin genes by the radiation-sensitive promoter Egr-1 in non-small cell lung cancer cell lines were observed. Immunodeficient mice (NOD/scid) subcutaneously implanted with A549 cells were treated by conventional radiotherapy (2Gy×6) and/or gene therapy (intratumor injection of adenovirus vectors Ad.Egr-wtp53-endostatin and Ad.CMV-sCAR-EGF 24 h before the first and fourth local doses). Immunologic mechanisms were explored.

**Results:** The fusion protein SCAR-EGF expressed from Ad.CMV-sCAR-EGF significantly increased infection efficiency of Ad.Egr-wtp53-endostatin in human non-small cell lung cancer cell lines. Cancer control was most significantly improved in the group receiving local radiotherapy combined with gene therapy as shown by prolongation of mean survival time by 75.2%, reduction in average tumor weight by 88.7%, decrease in pulmonary metastasis by 76.9% and decrease in intratumor angiogenesis by 80.4% as compared to local radiotherapy alone ( $P < 0.05$ ). Immunologic studies showed stimulated natural killer (NK) and cytotoxic T lymphocyte (CTL) activity as well as increased interferon- $\gamma$  (IFN- $\gamma$ ) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) secretion in this combined treatment group as compared with the group receiving local treatment alone ( $P < 0.05$ ).

**Conclusion:** The experimental findings in the present study showed that adenovirus vectors Ad.Egr-wtp53-endostatin and Ad.CMV-sCAR-EGF in combination with local radiotherapy could improve the tumor control. These observations may set the stage for developing clinical protocols with recombinant adenovirus-mediated gene-radiotherapy in non-small cell lung cancer.

#### EP-2032

Radiotherapy gets improved by a nanotechnology based enzyme therapy in glioblastoma primary cultures

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**Purpose or Objective:** One of the main effects of radiotherapy is the generation of free radicals as a consequence of the incidence of radiation on the aqueous molecules present in the cells. The enzyme D-amino acid oxidase (DAO) is also able to generate free radicals when converting D-amino acids in their corresponding cetoacids. Our principal aim is to increase radiotherapy effects, using